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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	**PAPER NUMBER**
1631	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/817,244	YAKHINI ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56,80-90 and 92-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56,80-90 and 92-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Applicants' amendments and request for reconsideration in the communication filed on 14 September 2010 are acknowledged and the amendments are entered.

Claims 1-56, 80-90, and 92-101 are pending and examined in the instant Office action.

Withdrawn Objections/Rejections

The objections of claims 38 and 84 because of informalities are withdrawn in view of amendments filed to the instant set of claims on 14 September 2010.

The rejections of claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 under 35 U.S.C. 102(b) as being anticipated by Cuticchia et al. [CABIOS, 1992, volume 8, pages 467-474] are withdrawn in view of arguments on pages 13-16 of the Remarks.

The rejection of claim 11 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied above in further view of Koleszar et al. [US Patent 6,519,583; issued 11 February 2003; filed 27 July 1999] is withdrawn in view of arguments on pages 18-19 of the Remarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejections are newly applied:

35 U.S.C. 103 Rejection #1:

Claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. [CABIOS, 1992, volume 8, pages 467-474].

Claim 1 is drawn to a computer-implemented method for overlaying gene- or protein-related data on chromosome maps to provide at least one data enhanced chromosome map as output. First, the method comprises receiving the chromosome

maps to a computer as a first input. Second, the method comprises receiving a list comprising a plurality of gene- or protein- related data items as a second input to a computer, each data item including data other than data specifying a genetic location on said chromosome maps. Third, the method comprises providing an identifier specifying a genetic location for each of the data items on the chromosome map. Fourth, the identifiers are matched with predefined identifiers on the chromosome maps. Fifth, the gene or protein data are re-ordered based on matching the identifiers to an order matching the predefined identifiers on the chromosome maps. Sixth, the biological data items are displayed on the at least one chromosomal map at locations determined by the reordered data items to provide data-enhanced output. All of the steps of this method are automated.

The article of Cuticchia et al. teaches the computer software CMAP, which is a contig mapping and analysis package and relational database for chromosome construction (see title). The computer apparatus (i.e. automation) aspect of the first step of inputting data is taught in the first two paragraphs under “System and methods” on pages 467 to 468 of Cuticchia et al. (automation) and column 1 on page 472 of Cuticchia et al. (first step). The second step of the instant claim is taught in some of the fields in Table I on page 468 of Cuticchia et al. wherein such fields as “Contig Order,” and “Active” are used for importing and teaching the locations of contigs (i.e. pieces of oligonucleotides) within the larger biomolecule or chromosome. The third step of the instant claim is taught in the full paragraph of column 2 on page 468 of Cuticchia et al. wherein additional data identifiers (not locations) such as differences in degrees of

hybridizations between clones in the chromosomes are input (i.e. "updated" in the computer). Figure 1 on page 468 of Cuticchia et al. teaches the fourth step of the instant claim wherein the hybridization data is matched within a matrix wherein each cell corresponds to a different location in the library chromosome data (Figure 2B of Cuticchia et al.). The fifth step of the instant claim of reordering the maps is taught in the section “Integration of Physical Maps” in the paragraph bridging columns 1-2 on page 473 of Cuticchia et al. wherein physical and chromosomal maps are merged based on their contents. Furthermore, the last paragraph of the introduction of Cuticchia et al. teaches ordering the data according to properties in the data fields. Figure 1 of Cuticchia et al. also acts as a display (sixth step) for a map of a chromosome that is enhanced with hybridization data.

While Cuticchia et al. does not teach direct inputting of chromosomal maps, the input data is described in the full paragraph on page 469 of Cuticchia et al. It is suggested (in the paragraph bridging pages 469 and 470 of Cuticchia et al.) that these input data correspond to chromosomal locations and oligonucleotide hybridizations via relational databases. Consequently, Cuticchia et al. suggests use of chromosomal mapping techniques to yield more information on chromosomes in the libraries of genomic data.

With regard to claim 2, Figure 1 on page 468 (and the GUI discussed on the same page) of Cuticchia et al. provides and interactive interface for selections of data

types to be displayed (see caption of Figure 1 of Cuticchia et al. which teaches how a user can select specific information from within the matrix).

With regard to claim 3, Figure 1 on page 468 of Cuticchia et al. also illustrates a spatial grouping of biological data of associated genes. It is suggested in the paragraph bridging pages 469-470 of Cuticchia et al. that these genes are associated with chromosomal locations.

With regard to claim 12, Figure 1 on page 468 of Cuticchia et al. teaches the matching of hybridization data obtained from a distinct source than the chromosome mappings that are suggested in the paragraph bridging pages 469-470 of Cuticchia et al.

With regard to claim 13, the data are selected from names of biomolecules published throughout the publication of Cuticchia et al.

With regard to claim 15, the title of Cuticchia et al. teaches use of a relational chromosomal database wherein as in Figure 1 of Cuticchia et al., the tables of hybridization data are cross-referenced with the chromosomal contig data. Additionally, the paragraph bridging pages 469 and 470 suggests a relational database that matches indices (i.e. the predefined identifier "L67A12") with the chromosomal location.

With regard to claims 20-22 and 55-56, Figure 1 of Cuticchia et al. compares co-location values of the cells in the matrix to by calculating for each cell, a statistically significant value of *d(a,b)* that assesses hybridization capacity (see full paragraph in column 2 on page 468 of Cuticchia et al. which teaches how differences in hybridization between clones are related to locations and overlap). These values of *d(a,b)* act as additional hybridization data that are used to annotate the location values of chromosomal data. Additionally, the full paragraph in column 2 on page 468 of Cuticchia et al. suggests that this additional data may be used to update fields in the relational databases. Consequently, these values of *d(a,b)* and D would be in effect displayed along side the location and identifier data as these data values are is a data file accompanying the gene display.

With regard to claim 24, the hybridization data of Figure 1 of Cuticchia et al. are interpreted to be relevance scores.

With regard to claim 26, Figure 1 of Cuticchia et al. is interpreted to be scatter plot data.

With regard to claim 27, a plurality of hybridization analyses are used to determine the gene and contig data of Figure 1 of Cuticchia et al.

With regard to claims 28-29, a map of the chromosome along with the degree of hybridization are displayed (i.e. as a heat map) in Figure 1 of Cuticchia et al. This heat map is interpreted to encompass annotations and statistical data.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the chromosomal data of Cuticchia et al. by inputting a map of specific genes to locations on chromosomes wherein the motivation would have been that giving chromosomal locations to genes in randomly organized libraries of genetic data gives a biological meaning to each gene in the mapping study from the initial steps of the process onwards [paragraph bridging pages 469-470 of Cuticchia et al. and Table I on page 468 of Cuticchia et al.].

Response to arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that Cuticchia et al. does not teach the first limitation of chromosomal maps being received as a first input. This argument is not persuasive because it is suggested that the data input into the study (full paragraph on page 469 of Cuticchia et al.) may be related via a relational database to other data corresponding location data (paragraph bridging pages 469-470 of Cuticchia et al.). Applicant next argues that since these chromosome maps are allegedly no taught, data enhanced chromosome maps and other identifiers corresponding to locations on the chromosome

maps are not taught. These arguments are not persuasive because, as explained above, the document of Cuticchia et al. teaches chromosomal mapping techniques.

Applicant further argues that Cuticchia et al. does not teach predefined identifiers. This argument is not persuasive because Cuticchia teaches matching hybridization data and Cuticchia et al. suggests mapping chromosomal location to genes with predefined identifiers specifying locations in the microarrays. For example, Figure 2B of Cuticchia et al. teaches the predefined identifier "L67A12" for a cloned gene. The paragraph bridging columns 1 and 2 on page 469 of Cuticchia et al. teaches that this identifier "L67A12" specifies the location of this clone is row A, column 12 of plate 67 within the Lorist sub-library of chromosomal data. The chromosomal location and hybridization data are then mapped to the gene corresponding with this predefined identifier "L67A12."

Applicant next argues that Cuticchia et al. does not reorder the data to an order matching the order of the predetermined identifiers. This argument is not persuasive because since the instant claims do not recite any specific order for the predefined identifiers, the claims are interpreted broadly such that ANY order of the predefined identifiers is the order of the predefined identifiers. As a result, the matching of hybridization data in Figure 1 of Cuticchia et al. is interpreted such that the data items (in this instance, the cells of the matrix) are reordered to match an order of the predefined identifiers. Additionally, the last paragraph of the introduction on page 467 of Cuticchia et al. teaches ordering data associated with chromosomal mapping.

With regard to claims 3, 12, and 15, applicant argues that since Cuticchia et al. does not teach chromosomal mapping, the further limitations of this set of claims are not met. These arguments are not persuasive because as discussed above, Cuticchia et al. suggests use of chromosomal mapping techniques.

With regard to claim 13, applicant argues that Cuticchia et al. does not teach genetic locations that are published. This argument is not persuasive because the bottom left column of Table I on page 468 of Cuticchia et al. teaches chromosomal locations (Chromosome 1-8) that are published within the article of Cuticchia et al.

With regard to claim 15, applicant argues that Cuticchia et al. does not teach matching location identifiers with the predefined identifiers. This argument is not persuasive because the paragraph bridging pages 469 and 470 suggests a relational database that matches indices (i.e. the predefined identifier "L67A12") with the chromosomal location.

With regard to claim 20, applicant argues that the co-location value is not statistically assessed with the co-location statistical significance values displayed along-side the genetic data. This argument is not persuasive because the co-location value *d(a,b)* is summed across the entire genome to define the statistical quantity D. This quantity, D, assess the overall statistical significance of overlap and is displayed as one of the fields in the relational database along with the other genetic identification data [full paragraph column 2 on page 468 of Cuticchia et al.].

With regard to claims 21-22, applicant argues that the "additional" information is not displayed along a chromosome map. This argument is not persuasive because, as

discussed above, Figure 1 of Cuticchia et al. is a chromosome map annotated/enhanced with hybridization data. Additionally, the full paragraph in column 2 on page 468 of Cuticchia et al. suggests that this additional data may be used to update fields in the relational databases. Consequently, these values of *d(a,b)* and D would be in a data file accompanying the gene (in effect displayed along side the location and identifier data).

With regard to claim 24, applicant argues that relevance scores do not encompass hybridization data. This argument is not persuasive because the degree of hybridization and expression of a clone in Figure 1 of Cuticchia et al. is interpreted to be related to a measure of the relevance (i.e. probability of hybridization and expression) of the probe in the system.

With regard to claim 26, applicant argues that Figure 1 of Cuticchia et al. is not a scatter plot because the proper data is not being displayed. This argument is not persuasive because claim 26 only requires that gene or protein related data be displayed in the form of a scatter plot; claim 26 does not limit which type of genetic or proteomic data to be displayed.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #2:

Claims 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 above

in further view of Koleszar et al. [US Patent 6,519,583; issued 11 February 2003; filed 27 July 1999].

Claims 4-10 are dependent from claim 1 with the additional features of displaying the genetic data is a specific means wherein each claim identifies a separate feature used to display the data.

Cuticchia et al. makes obvious the computer-implemented methods for overlaying gene related data on chromosomal maps, as discussed above.

Cuticchia et al. does not explicitly state that every step corresponding to the instant claims with regard to the required display techniques.

The invention of Koleszar et al., entitled, "Graphical viewer for biomolecular sequence data," states in the abstract:

> Disclosed are methods, media and systems for graphically displaying computer-based biomolecular sequence information. Generally, biomolecular sequence information may be graphically depicted in a variety of different forms in accordance with the present invention. The sequence information may be composed of nucleotide or amino acid sequence information or both. The graphical depictions may be in several different formats providing different information relating to the sequences, and may be displayed in one or more screens of a computer user interface.

Figure 4A of Koleszar et al. has the ability to zoom in on regions or zooming out and compressing regions of the genomic sequence of interest as is illustrated on the toolbar of the schematic with pop-up buttons to control the viewing of the features. By zooming into a section of the plot, other sections are cut out of the viewing region (see Figure 4B of Koleszar et al.). Figure 4B of Koleszar et al. also illustrates multiple portions of the chromosome at different magnifications viewed simultaneously. Figure 4B of Koleszar et al. also displays on the same plot both a high (magnified) and mid level view of the plurality of chromosome maps. Additionally, the middle panel of Figure

4B of Koleszar et al. illustrates a detailed view with detailed information on the chromosome map; these high-level, mid-level, and detailed views are interlinked so that the changes in one view changes the other views substantially simultaneously. Tool-tips are displayed at the tops of Figures 4A and 4B.

The purpose of Koleszar et al. in explained in column 2, lines 5-9, which states:

> Accordingly, the development if a display tool which allows a user to clearly and effectively display gene loci information for a given organism or organisms and/or other biomolecular sequences in desirable.

Consequently, Koleszar et al. describes a user friendly, convenient, and effective display of gene loci information.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the chromosomal maps and matrices of Cuticchia et al. by use of the display techniques of Koleszar et al. wherein the motivation would have been that Koleszar et al. has the advantage of displaying the genomic data in a more convenient and user-friendly format [see, for example, column 2, lines 5-9 of Koleszar et al.].

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that the reference of Koleszar et al. does not overcome the alleged deficiencies of Cuticchia et al. This argument is not persuasive because the

combination of Cuticchia et al. and Koleszar et al. teaches the required the limitations in the instant set of claims.

With regard to claim 5, applicant argues that there is no advantage of "zooming" (as illustrated in Koleszar et al.) into Figure 1 of Cuticchia et al. because Figure 1 of Cuticchia et al. is already visible. This argument is not persuasive because the motivation to combine Cuticchia et al. and Koleszar et al. is to make the data more user-friendly and user-accessible- and not to make invisible data visible. Consequently, Koleszar et al. makes the data of Cuticchia et al. more user-accessible and convenient by enlarging the data matrix.

Applicant next argues with regard to claim 7 that since Figure 1 of Cuticchia et al. is not a chromosomal map, zooming into a chromosomal map (as is accomplished in Koleszar et al.) is not combinable with Figure 1 of Cuticchia et al. This argument is not persuasive because, as discussed above, Figure 1 of Cuticchia et al. is associated with data that maps genes to chromosomes.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #3:

Claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Schena et al. [PNAS, 1996, volume 93, pages 10614-10619].

Claim 14 is further limiting comprising using official standard gene names.

The article of Cuticchia et al. suggests mappings of data onto chromosomal maps, as discussed above.

While Cuticchia et al. does not demonstrate official standard names, Schena et al. uses accession numbers in Table 1 on page 10616. The article of Schena et al. studies parallel human genome analysis and microarray based expression monitoring of 1000 genes.

Claims 16-17 is further limiting wherein the biomolecule data comprises a plurality of matrices of gene expression data. While Cuticchia et al. teaches matrices of chromosomal data, these matrices do not comprise gene expression data. The article of Schena et al. illustrates matrices of gene expression data in Figure 1 wherein the rows and columns correspond to genes and experiments.

Claims 18-19 are further limiting wherein the rows and columns of the gene expression data are associated with a particular gene and experiment. As explained above, the article of Schena et al. illustrates matrices of gene expression data in Figure 1 wherein the rows and columns are associated with genes and experiments.

Claim 23 is further limiting wherein the annotations comprise gene ontology. Schena et al. teaches that the ontology of a portion of the genes is from the genus *Arabidopsis* in the first full paragraph of column 2 on page 10614 of Schena et al.

Additionally, Schena et al. lists Blast identification numbers and gene accession numbers for a subset of the cells in Table 1.

Claim 25 is further limiting wherein the data is displayed on a single matrix and the additional data is displayed on a second matrix.

Figure 1 of Schena et al. comprises two matrices. The first matrix (left panel) corresponds to gene data in a control; the second, matrix (right panel) corresponds to additional gene data wherein the microarray is exposed to heat shock.

Claims 30-33 are further limiting wherein data for the rows of each matrix are calculated, and an auxiliary process is used to obtain cluster data. The results are displayed along side the matrices (i.e. as a heat map with color coding, in a column adjacent to the matrices, or in multiple columns next to the matrices).

Figure 1 of Schena et al. teaches a heat map wherein the colors of the cells within the matrix are interpreted to represent cluster data for each row. The cluster data for each panel for Figure 1 of Schena et al. is subtracted in order to display the resultant cluster data in the form of the matrix in the left panel of Figure 2 of Schena et al. The colors in the heat map of Figure 2 of Schena et al. are governed by the thresholds in the row underneath the figure. Figure 2 of Schena et al. is comprised of a multicolumn matrix of cluster data based on the ratios of the left and right panels of Figure 1 of Schena et al. displayed adjacent to Figure 1 of Schena et al. This multicolumn matrix is

comprised of a series of single columns used to assess the ratios of the series of single columns in Figure 1 of Schena et al.

Claim 34 is further limiting wherein the biomolecular data comprises a microarray of gene expression data, wherein each row is associated with a gene and each column is associated with an experiment. A portion of each matrix is associated with normal tissue and another portion is associated with abnormal tissue.

Cuticchia et al. does not teach gene expression data and resulting matrices.

Figure 1 on page 10615 of Schena et al. illustrates two microarrays of gene expression data; the left matrix of data is normal (-Heat Shock), and the right matrix is abnormal (+Heat Shock). Each row and column of the matrices in Figure 1 of Schena et al. is associated with a gene and an experiment.

With regard to claims 35 and 40, the data in Figure 1 of Schena et al. are displayed in terms of color-coded heat maps.

With regard to claims 36 and 82, relevance scores comparing normal (-Heat Shock) to abnormal (+Heat Shock) are displayed as differential expression profiles in Figure 2A of Schena et al.

With regard to claim 37, Cuticchia et al. teaches use of a GUI to display maps in column 2 on page 468.

With regard to claims 41 and 87, the relevance scores of Figure 2 of Schena et al. are displayed as a heat map that is “binary" in that for expression ratios between 0.5 and 2.0, the color of the cell on the microarray is dark- otherwise, the cell on the microarray is light.

With regard to claims 42 and 88, the shadings in Figure 1 of Cuticchia et al. are interpreted to teach use of density scores, as they are based on genes with suggested chromosomal locations, hybridization distances *d(a,b),* and success in expression. For example, the color of the shadings of Figure 1 of Cuticchia et al. demonstrates that the colors white and black signify success and failure of hybridization, respectively. Additionally, the color gray indicates lack of a gene (i.e. no expression of a clone). Consequently, the density scores of Figure 1 of Cuticchia et al. relate to a suggestion of chromosomal location, degree of hybridization overlap, and success in gene expression.

With regard to claims 43 and 89, Schena et al. teaches thresholds as the basis for coloring the relevance scores (differential expression profiles of Figure 2 of Schena et al.) in the legend to Figure 2 of Schena et al. This color coding by interval acts to filter data by relevance score (i.e. differential expression value).

Independent claim 80 is drawn to similar subject matter as dependent claim 34, except in independent form. As claim 34 is taught in Cuticchia et al. and Schena et al., independent claim 80 is also taught.

With regard to claim 81, Figure 1 of Schena et al. is interpreted to be a heat map.

With regard to claims 83 and 86, the relevance scores for Figure 1 of Schena et al. are interpreted to be the differential expression profiles in Figure 2A of Schena et al. Figure 2A of Schena et al. is also interpreted to be a heat map.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the chromosomal maps and matrices of Cuticchia et al. by use of the control and abnormal microarrays of Schena et al. wherein the motivation would have been that the normal vs. heat shock microarray profiles in Figures 1 and 2 of Schena et al. provide an application of the array and mapping analyses of Cuticchia et al. in that specific differences between corresponding genes in microarrays are assessable in the presence and absence of an abnormal condition (heat shock). Furthermore, the additional data fields listed in Table I of Cuticchia et al. would enhance the microarray data of Figures 1 and 2 of Schena et al. by annotating each cell with more information than merely expression level/ratio.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the chromosomal maps and matrices of Cuticchia et al. by

use of the pluralities of gene expression matrices and gene expression differential matrices as in Schena et al. because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the gene expression profile matrices of Schena et al. are an alternate form of displaying data related to a gene on a chromosome than the gene hybridization and clone expression data of Cuticchia et al. There would have been a reasonable expectation of success in combining the studies of Schena et al. and Cuticchia et al. because both studies analogously pertain to viewing data regarding chromosomal properties in the form of matrices.

Response to arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that the reference of Schena et al. does not overcome the alleged deficiencies of Cuticchia et al. This argument is not persuasive because the combination of Cuticchia et al. and Schena et al. teaches the required the limitations in the instant set of claims.

With regard to claim 14, applicant argues that the identifiers allegedly taught in claim 13 (i.e. “L67A12"), do not correspond to the recited identifiers of claim 13. Therefore, applicant argues, since claim 13 is allegedly not taught in Cuticchia et al., neither is claim 14. This argument is not persuasive because the bottom left column of Table I on page 468 of Cuticchia et al. teaches chromosomal locations (Chromosome 1-8) that are published within the article of Cuticchia et al.

With regard to claim 16, applicant argues that Figure 1 of Schena et al. does not teach a particular gene in each row of the microarray and a particular sample in each column of the microarray. This argument is not persuasive because it is not commensurate with the limitations recited in instant claim 16. Claim 16 uses open language to recite that each row contains data values for a particular gene or protein and each column and that the results for each measured sample are provided in the columns of the microarray. Figure 1 of Schena et al. comprises at least one particular gene in each row of the microarray. Additionally, since the term "sample" is not limited to a gene or protein, each column of the microarrays corresponds to a sample comprised of *Arabidopsis* biomolecules. Consequently, the intersection of each row and column in Figure 1 of Schena et al. maps to a plurality of data values (one colored data value in the left microarray and another data value in the right microarray). Furthermore, the intersection of each row and column comprises data related to a particular gene and a particular sample (an *Arabidopsis* sample).

With regard to claim 17, applicant argues that since expression matrices are already identified as chromosome maps, the same matrix cannot be used to identify the claimed gene or protein data. This argument is not persuasive because while Cuticchia et al. suggests chromosome maps, Figure 1 of Schena et al. illustrates a plurality of gene related data. Consequently, the combination of Cuticchia et al. and Schena et al. teaches all of the limitations of the instantly rejected claim.

With regard to claim 18, applicant reiterates the arguments for claim 16. This argument is not persuasive because claim 18 uses the open language that each row is

ASSOCIATED with a particular gene. Since each row of the microarrays in Figure 1 of Schena et al. is from *Arabidopsis*, each row of Figure 1 of Schena et al. is ASSOCIATED with each gene in *Arabidopsis*.

With regard to claim 23, applicant argues that neither Cuticchia et al. nor Schena et al. teaches annotations with gene ontology information. This argument is not persuasive because Table 1 on page 10616 of Schena et al. annotates the microarray of Figure 1 with gene ontology information comprising the Blast identity and the Accession numbers of each of the genes related to *Arabidopsis.*

With regard to claim 30, applicant argues that Figures 1 and 2 of Schena et al. do not teach displaying cluster data along side a display. This argument is not persuasive because the two dimensional matrices of Figures 1 and 2 of Schena et al. are comprised of row vectors and column vectors. Furthermore, the row vectors in Figure 2 of Schena et al. are derived by taking the ratios of the corresponding cells (within the same row vector) with and without heat shock, respectively. Consequently, the ratios in Figure 2 of Schena et al. comprise cluster data that are displayed along side the plots of Figure 1 of Schena et al.

With regard to claims 32 and 33, applicant argues that a matrix with column(s) and with cluster data displayed adjacent to the matrix is not present in Schena et al. This argument is not persuasive because Figures 1 and 2 of Schena et al. are multi-column matrices with the level of gene expression (i.e. cluster data) displayed adjacent to (i.e. on top of) the matrix using a series of colors. Displaying this cluster data on top

of the microarray data is an obvious variant of displaying the data adjacent to the microarray.

With regard to claim 34, applicant first reiterates the arguments pertinent to claims 16 and 18. Next, applicant argues that while Figure 1A of Schena et al. is not conducted on heat shock tissue and Figure 1B of Schena et al. is conducted on heat shock tissue, there is no explicit statement in Schena et al. demonstrating that this study is conducted on normal vs. abnormal tissue. Next, applicant argues that a single matrix is not divided into two smaller matrices wherein one of the matrices pertains to healthy tissue and the second pertains to unhealthy tissue. This argument is not persuasive because the caption to Figure 2 of Schena et al. as well as the first paragraph in column 2 on page 10615 of Schena et al. teaches that Figure 2A of Schena et al. is obtained by taking respective ratios of corresponding cells from Figure 1A to Figure 1B of Schena et al. Additionally, in the absence of a definition of "experiment," each cell on each microarray in Figure 1 of Schena et al. is interpreted to encompass an individual experiment. Additionally, in the absence of a definition of normal vs. abnormal tissue, Figure 1A of Schena et al. is interpreted to be conducted on normal tissue in that the tissue is not undergoing heat shock, and Figure 1B of Schena et al. is interpreted to be conducted on abnormal tissue in that the tissue is undergoing heat shock. Additionally, it is interpreted that the two microarrays in Figure 1 of Schena et al. (wherein the left microarray is the normal array and the right microarray is the abnormal microarray) are obvious variants of a single microarray divided into two separate microarrays.

With regard to claim 36, applicant argues that Figure 2A of Schena et al. does not teach relevance scores that are along side the microarray data of Figure 1 of Schena et al. In the absence of a limiting definition of "along side," displaying the relevance scores in a consecutive figure is interpreted to be an obvious variant of "along side."

With regard to claim 41, applicant argues that binary codes are not taught in Cuticchia et al. of Schena et al. This argument is not persuasive because the relevance scores of Figure 2 of Schena et al. are displayed as a heat map that is "binary" in that for expression ratios between 0.5 and 2.0, the color of the cell on the microarray is dark- otherwise, the cell on the microarray is light.

With regard to claim 42, applicant argues that the limitations regarding density scores are not taught. This argument is not persuasive because (as explained above) the shadings in Figure 1 of Cuticchia et al. are interpreted to teach use of density scores, as they are based on genes with suggested chromosomal locations, hybridization distances *d(a,b),* and success in expression. For example, the color of the shadings of Figure 1 of Cuticchia et al. demonstrates that the colors white and black signify success and failure of hybridization. Additionally, the color gray indicates lack of a gene (i.e. no expression of a clone). Consequently, the density scores of Figure 1 of Cuticchia et al. relate to a suggestion of chromosomal location, degree of hybridization overlap, and success in gene expression. This plot (Figure 1 of Cuticchia et al.) relates the Figures 1 and 2 of Schena et al. because just as Figures 1 and 2 and Table 1 of Schena et al. plot success and failure of gene expression and relationships with location

and ontology in the *Arabidopsis*, Figure 1 and Cuticchia et al. analogously relates success in expression and hybridization with a suggested chromosomal location. In this absence of a teaching of "density score" in the specification, the heat map in Figure 1 of Cuticchia et al. is interpreted to encompass the meaning of density scores.

With regard to claim 43, applicant argues that Figure 2 of Schena et al. does not teach excluding a set of data in the array below a specific threshold. This argument is not persuasive because the claims do not recite excluding- the claim only recite filtering. Consequently, by coloring the cells with expression ratios less than 0.5 light and those with higher expression ratios (0.5 to 2.0) dark, it is interpreted that Schena et al. is filtering out the data with low expression ratios/relevance scores. It is noted that in view of this OBVIOUSNESS rejection, the boundaries of these intervals act as thresholds for differentiating (and filtering) data according to the interval in which the data is located.

With regard to claim 80 (dependent claim 34 is independent form), applicant reiterates the arguments for claim 34. For the reasons discussed above for claim 34, these arguments are not persuasive.

With regard to claim 82 (reciting the subject matter of claim 36, but dependent from claim 80), claim 87 (reciting the subject matter of claim 41, but dependent from claim 82), and claims 88-89 (reciting the subject matter of claims 42-43, but dependent from claim 82), applicant reiterates arguments addressed above for claims 36 and 41-43. For the reasons discussed above, these arguments are not persuasive.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #4:

Claims 38 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982].

Claims 38 and 84 are further limiting comprising a "p value."

Cuticchia et al. and Schena et al. make obvious an automated method for mapping genetic information, as discussed above.

Cuticchia et al. and Schena et al. do not use a p-value.

The invention of McCully studies the therapeutic effects of salts as anti-neoplastic agents.

Specifically, example 7 in columns 8-9 of the invention uses a statistical technique to evaluate the effectiveness of the salts in malignancies in mice. Line 60-65 of column 8 of McCully state that the p values can be used to calculate differences between control and experimental samples in mice. This p value acts as a statistical cut off for determining deviation between a control and experimental sample.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromosomal ordering maps and matrices of Cuticchia et al. and Schena et al. by use of the statistical criteria of McCully because it is obvious to use a known technique to improve a similar method. In this instance, the use of the statistical criteria of McCully to analyze the arrays of Partridge et al. would have resulted in improved and more advanced statistical analysis. There would have

been a reasonable expectation of success in combining these sources because the statistical techniques of McCully are generally applicable to the analysis of the other references.

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that the reference of McCully does not overcome the alleged deficiencies of Cuticchia et al. and Schena et al. This argument is not persuasive because the combination of Cuticchia et al., Schena et al., and McCully teaches the required the limitations in the instant set of claims.

Applicant additionally argues that Figure 2A of Schena et al. does not teach relevance scores that are along side the microarray data of Figure 1 of Schena et al. In the absence of a limiting definition of "along side," displaying the relevance scores in a consecutive figure is interpreted to be an obvious variant of "along side." Furthermore the expression level ratios of Figure 2A of Schena et al. represent differences in expression probabilities for normal vs. heat shocked samples. Consequently, the heat map of Figure 2A of Schena et al. comprises an alternative to the p values as relevance scores that are disclosed in paragraph 94 of the specification.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #5:

Claims 39 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378].

Claims 39 and 85 recite either use of line maps.

Cuticchia et al. and Schena et al. make obvious an automated method or mapping genetic information, as discussed above.

Cuticchia et al. and Schena et al. do not teach line maps.

The article of Ben-Dor et al. studies radiation hybrid ordering.

Specifically, Figure 6 illustrates line maps indicating scores and distances between the relevant markers.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromosomal ordering maps and matrices of Cuticchia et al. and Schena et al. by use of chromosomal mapping techniques (i.e. line maps) of Ben-Dor et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the line maps and the densities of Ben-Dor et al. are an alternate means of analyzing the mappings of chromosomes. There would have been a reasonable expectation of combining Cuticchia et al. and Schena et al. with Ben-Dor et al. because they all pertain to analogous subject matter of chromosomal mapping.

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that the reference of Ben-Dor et al. does not overcome the alleged deficiencies of Cuticchia et al. and Schena et al. This argument is not persuasive because the combination of Cuticchia et al., Schena et al., and Ben-Dor et al. teaches the required the limitations in the instant set of claims.

Applicant additionally argues that there is no advantage or motivation for choosing line maps as opposed to the numerous other means for mapping chromosomes. This argument is not persuasive because as line maps are an alternate means for mapping the same information using a substitute (art accepted equivalents), it is adequate for an obviousness prior art rejection. There is a reasonable expectation of success in combining Cuticchia et al., Schena et al., and Ben-Dor et al. because all three studies pertain to means for mapping chromosomal data.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #6:

Claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of Pollack et al. [Nature Genetics, volume 23, 1999, pages 41-46].

Claims 44 and 90 are further limiting wherein matching chromosomal copy abnormality data with the gene related data identifiers and displaying this data along side the gene-related data.

Claims 46-47 and 92-93 are further limiting wherein the chromosomal copy number information is interlaced and the chromosomal copy number is displayed in color on heat maps.

Claim 49 is further limiting with the additional limitations of having third and fourth matrices each represented by chromosomal abnormality values.

Claim 45 is further limiting wherein one-to-one matching is executed between the cells of the third matrix (chromosomal copy numbers) to the first matrix and from the fourth matrix to the second matrix.

Claim 52 is further limiting wherein the chromosomal copy matrices are in the form of heat maps.`

Claim 101 is an independent claim drawn to similar subject matter as dependent claim 49, except as an independent claim.

Claim 98 is further limiting wherein the matrices are in the form of heat maps.

Claims 53-54 and 99-100 are further limiting with density scores and relevance scores that are based on genetic locations, identifiers, and thresholds.

Cuticchia et al. makes obvious enhanced mapping of data onto chromosomal maps, as discussed above. The shadings in Figure 1 of Cuticchia et al. are interpreted to teach use of density scores, as they are based on locations, expression of clones, and hybridization distances *d(a,b)*. The color of the shadings of Figure 1 of Cuticchia et

al. demonstrate intervals of hybridization and expression corresponding to different density scores (i.e. the colors white and black signify success and failure of hybridization; the color gray indicates lack of expression of a clone). Additionally, Cuticchia et al. provides a means for annotating or "interlacing" the suggested chromosomal mapping analyses with 1024 bytes of information explaining abnormalities (i.e. chromosomal copy numbers) [see paragraph bridging columns 1-2 on page 471 of Cuticchia et al.]

However, Cuticchia et al. does not teach abnormal copy numbers, or the one-to-one correspondences between the third and fourth matrices and the first and second matrices, respectively.

Schena et al. teaches separate gene expression matrices under abnormal and normal conditions. Specifically, Figure 1 of Schena et al. illustrates two matrices of gene expression under normal [-heat shock] and abnormal [+heat shock] conditions. Schena et al. continue the same analysis with normal [-phorbol ester] and abnormal [+phorbol ester], respectively [data not shown]. However, Figure 2 illustrates a "third" matrix related to heat shock (left) and a "fourth" matrix related phorbol ester (right). Each matrix in Figure 2 of Schena et al. corresponds to a one-to-one ratio between the cells in the original two matrices (i.e. normal vs. abnormal- cell by cell) from which a differential is measured to generate values for each of the cells in Figure 2 of Schena et al. Also, as explained above, the legend of Figure 2 of Schena et al. teaches relevance score and their thresholds used to encode for different range of relevance scores in Figure 2.

However, Schena et al. does not teach that these additional matrices are related to chromosomal copy numbers.

The article of Pollack et al. studies genome-wide analysis of DNA copy-number changes using cDNA microarrays.

Specifically, Figure 5a on page 44 of Pollack et al. illustrates a color coded heat map (red and green) for determining the genetic states of normal vs. diseased breast cancer samples. Rather than plotting expression and hybridization on an enhanced array image (as in Figure 1 of Cuticchia et al.) or differential expression patterns between control and abnormal arrays (Figures 1 and 2 of Schena et al.), Pollack et al. plots expression of genes of control and abnormal tissue arrays adjacent to matrices with the corresponding copy number data (Figure 5 of Pollack et al.).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromosomal mapping techniques of Cuticchia et al. and Schena et al., by use of the color coded heat map plots of Pollack et al. wherein the motivation would have been that the use of such plots allow more conveniently acquired and well resolved data [see lines 13-17 of abstract on page 41 and Figure 5a of Pollack et al.] It would have been further obvious to modify differential gene expression to analyze abnormalities as in Cuticchia et al. and Schena et al. by interlacing the disease analysis by chromosomal copy number analysis as in Pollack et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, abnormality analysis by chromosomal copy analysis in matrices is an alternate form of abnormality analysis by measuring differential expression analysis. There would

have been a reasonable expectation of success in combining Cuticchia et al., Schena et al., and Pollack et al. because all three of the studies analogously rely on comparison of array data to determine genetic abnormalities.

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first reiterates arguments that the reference of Pollack et al. does not overcome the alleged deficiencies of Cuticchia et al. and Schena et al. This argument is not persuasive because the combination of Cuticchia et al., Schena et al., and Pollack et al. teaches the required the limitations in the instant set of claims.

With regard to claim 45, applicant argues that Figure 1 and 2 of Schena et al. do not demonstrate the associations (i.e. between rows and columns of the first and third matrices or the rows and columns of the second and fourth matrices) recited in the instantly rejected claim. This argument is not persuasive because the same microarray preparation is used for each of the four microarrays (see "Microarray Preparation" [singular]) in column 2 on page 10614 of Schena et al. In other words, the same microarray setup is used four times (no Heat shock, Heat Shock, no Phorbol ester, phorbol ester). Thus, each of the four microarray setups corresponds to one of the four matrices wherein the location for each cell (i.e. row, column) within the microarray setup corresponds to the same gene expression analysis in each of the four matrices. Applicant argues that while Schena teaches a third matrix (Figure 2A) that takes ratios

of the control to heat shock matrices at each cell and a fourth matrix (Figure 2B) that takes a ratio of the control to the phorbol ester matrices respectively, Schena et al. does not match the third matrix to the first matrix or the fourth matrix to the second matrix as required in the instant set of claims. This argument is not persuasive because Figure 2 MATCHES all of the matrices by plotting the expression ratios from all of the respective microarrays adjacent to one another.

With regard to claims 46 and 92, applicant argues that Cuticchia et al. does not teach the interlacing of chromosomal copy data with the data matrices. This argument is not persuasive because Cuticchia et al. teaches the ability to annotate chromosomal files with abnormality information- page 471 of Cuticchia et al. It is interpreted that annotating a matrix of data with relevant data files is a means of data enhancement that is an obvious variant of interlacing the data with the data filed on the plot itself. Furthermore, Pollack et al. teaches plotting a microarray of gene expression in the right panel of Figure 5a (analogous to the gene expression microarrays of Figure 2 of Schena et al.) adjacent a copy number matrix in the left panel of Figure 5a. Consequently, the combination of Cuticchia et al., Schena et al., and Pollack et al. make obvious interlacing chromosomal copy data with gene expression data in data files.

With regard to claims 53-54 (reciting the subject matter of claims 42-43, but dependent from claim 49), applicant reiterates arguments addressed above for claims 42-43. For the reasons discussed above, these arguments are not persuasive.

With regard to claim 101 (similar to dependent claim 45 is independent form), applicant reiterates the arguments for claim 45. For the reasons discussed above for claim 45, these arguments are not persuasive.

With regard to claims 95 and 98-100 (reciting the subject matter of claims 36, 39, and 42-43, but dependent from claim 10), applicant reiterates arguments addressed above for claims 36, 39, and 42-43. For the reasons discussed above, these arguments are not persuasive.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #7:

Claims 50 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982].

Claims 50 and 96 are further limiting comprising a “p value.”

Cuticchia et al., Schena et al., and Pollack et al. make obvious an automated method for mapping genetic information using chromosomal copy data, as discussed above.

Cuticchia et al., Schena et al., and Pollack et al. do not use a p-value.

The invention of McCully studies the therapeutic effects of salts as anti-neoplastic agents.

Specifically, example 7 in columns 8-9 of the invention uses a statistical technique to evaluate the effectiveness of the salts in malignancies in mice. Line 60-65 of column 8 of McCully state that the p values can be used to calculate differences between control and experimental samples in mice. This p value acts as a statistical cut off for determining deviation between a control and experimental sample.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromosomal ordering maps and matrices of Cuticchia et al., Schena et al., and Pollack et al. by use of the statistical criteria of McCully because it is obvious to use a known technique to improve a similar method. In this instance, the use of the statistical criteria of McCully to analyze the arrays of Partridge et al. would have resulted in improved and more advanced statistical analysis. There would have been a reasonable expectation of success in combining these sources because the statistical techniques of McCully are generally applicable to the analysis of the other references.

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant first argues that the reference of McCully does not overcome the alleged deficiencies of Cuticchia et al., Schena et al., and Pollack et al. This argument is not persuasive because the combination of Cuticchia et al., Schena et al., Pollack et al., and McCully teaches the required the limitations in the instant set of claims.

Applicant additionally argues that Figure 2A of Schena et al. does not teach relevance scores that are along side the microarray data of Figure 1 of Schena et al. In the absence of a limiting definition of "along side," displaying the relevance scores in a consecutive figure is interpreted to be an obvious variant of "along side." Furthermore the expression level ratios of Figure 2A of Schena et al. represent differences in expression probabilities for normal vs. heat shocked samples. Consequently, the heat map of Figure 2A of Schena et al. comprises an alternative to the p values as relevance scores that are disclosed in paragraph 94 of the specification.

The following rejections are reiterated:

35 U.S.C. 103 Rejection #8:

Claims 48, 51, 94, and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378].

Claims 48, 51, 94, and 97 recite either use of line maps.

Cuticchia et al., Schena et al., and Pollack et al. make obvious an automated method for mapping genetic information, as discussed above.

Cuticchia et al., Schena et al., and Pollack et al. do not teach line maps.

The article of Ben-Dor et al. studies radiation hybrid ordering.

Specifically, Figure 6 illustrates line maps indicating scores and distances between the relevant markers.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromosomal ordering maps and matrices of Cuticchia et al., Schena et al., and Pollack et al. by use of chromosomal mapping techniques (i.e. line maps) of Ben-Dor et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the line maps and the densities of Ben-Dor et al. are an alternate means of analyzing the mappings of chromosomes. There would have been a reasonable expectation of combining Cuticchia et al., Schena et al., and Pollack et al. with Ben-Dor et al. because they all pertain to analogous subject matter of chromosomal mapping.

Response to Arguments:

Applicant's arguments filed 14 September 2010 have been fully considered but they are not persuasive.

Applicant argues that the reference of Ben-Dor et al. does not overcome the alleged deficiencies of Cuticchia et al., Schena et al., and Pollack et al. This argument is not persuasive because the combination of Cuticchia et al., Schena et al., Pollack et al., and Ben-Dor et al. teaches the required the limitations in the instant set of claims.

Applicant additionally argues that there is no advantage or motivation for choosing line maps as opposed to the numerous other means for mapping chromosomes. This argument is not persuasive because as line maps are an alternate

means for mapping the same information using a substitute (art accepted equivalents), it is adequate for an obviousness prior art rejection. There is a reasonable expectation of success in combining Cuticchia et al., Schena et al., Pollack et al., and Ben-Dor et al. because all three studies pertain to means for mapping chromosomal data.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #9:

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Koleszar et al. as applied to claims 1-10, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Corcoran et al. [US PGPUB 2003/0224419; published; December 2003; filed 2 April 2003; benefit date 1 September 2000].

Claim 11 is further limiting comprising displaying popup dialogs to display additional details relative to a selected portion of the display.

Cuticchia et al. and Koleszar et al. make obvious computer-implemented methods for overlaying gene related data on chromosomal maps and then visualizing the biological data, as discussed above.

While Koleszar et al. has the ability to zoom in on regions or zooming out and compressing regions of the genomic sequence of interest as is illustrated on the toolbar of the schematic with pop-up buttons to control the viewing of the features, Cuticchia et al. and Koleszar et al. do not explicitly teach use of popup dialogs.

The document of Corcoran et al. teaches an analysis and visualization system for DNA sequencing [title]. Specifically, paragraph 132 of Corcoran et al. teaches use of popup dialog boxes as means for checking the status of the sequencing data.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the chromosomal maps and displays of Cuticchia et al. and the menus for viewing the structures of Koleszar et al. by use of the popup dialog boxes of Corcoran et al. because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the popup dialogs of Corcoran et al. are an alternate form of viewing the data than the tools of Cuticchia et al. and Koleszar et al. There would have been a reasonable expectation of success in combining Cuticchia et al., Koleszar et al., and Corcoran et al., because all three documents pertain analogously to interactive viewing of biological data.

Response to Arguments:

This is a new rejection.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Russell S. Negin/
Examiner, Art Unit 1631
5 October 2010